

## **REMARKS**

Claims 22-58 are currently pending. Claims 1-21 were previously cancelled without prejudice or disclaimer as to the subject matter of the cancelled claims. Claims 23, 26, 36, and 45-47 are cancelled herein without prejudice or disclaimer as to the subject matter of those cancelled claims. Applicants respectfully reserve the right to pursue the subject matter of the cancelled claims in one or more Continuation or Divisional applications. Claims 22, 31-35, 37-44, and 48-55 are amended herein. Support for the instant claim amendments can be found throughout the application as originally filed, *inter alia*, in paragraphs [57], [58], and [66]-[70]. Accordingly, Applicants submit that no new matter has been introduced into the application by way of the instant claim amendments. On entry of the instant claim amendments, claims 22, 24, 25, 27-35, 37-44, and 48-58 will be pending.

### **Objections**

Claim 46 was objected to for the recitation of “are maintain”. Applicants appreciate the Examiner’s notation of this grammatical error, and have addressed this objection in the instant claim amendments.

### **Rejections**

#### ***35 U.S.C. § 112, 1<sup>st</sup> Paragraph - Written Description***

Claims 22-58 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly failing to comply with the written description requirement. More specifically, it is asserted in the Office Action that the original claims and the originally filed specification only provide support for mating two haploid cells, wherein each haploid cell comprises one expression vector, each of which encodes one subunit of a heteromultimeric protein, for a total of two subunits. It is also asserted in the Office Action that the supporting disclosure for claims 36-44 and 48-55 includes the term “about” with respect to the claimed values.

Applicants respectfully disagree and traverse this rejection. Nevertheless, in order to expedite prosecution on the merits, Applicants have addressed each of these grounds of rejection in the instant claim amendments. For example, the subject matter of cancelled claim 23 is incorporated by amendment into amended claim 22. Cancelled claim 23 included the following recitation: "... by mating or fusing a first haploid *Pichia* cell containing a first expression construct, said first expression construct comprising nucleic acid sequences encoding for the expression of at least one subunit of said heteromultimeric polypeptide, operably linked to a first yeast promoter; and a second haploid *Pichia* cell containing a second expression construct, said second expression construct comprising nucleic acid sequences encoding for the remaining subunit(s) of said heteromultimeric polypeptide, operably linked to a second yeast promoter."

Each of the pending claims 35-44 and 48-55 has been amended to incorporate the term "about" in association with the recited numerical values.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 22-58 under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly failing to comply with the written description requirement.

### **35 U.S.C. § 112, 1<sup>st</sup> Paragraph - Enablement**

Claims 36-55 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly failing to comply with the enablement requirement. Applicants note with appreciation the Examiner's acknowledgement that the specification is enabling for a method of production of antibodies in diploid *Pichia* cells. See Office Action, page 5. While respectfully not acquiescing in the merits of the rejection as it applies to other heteromultimeric polypeptides, and for the purpose of expediting prosecution on the merits, Applicants have amended claim 22 herein to recite in pertinent part that the heteromultimeric polypeptide "... is an antibody or an antigen binding antibody fragment." Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 36-55 under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully reserve the right to address the issue of enablement of other heteromultimeric polypeptides in one or more Continuation or Divisional applications.

**35 U.S.C. § 112, 2<sup>nd</sup> Paragraph**

Claims 22-58 were variously rejected under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph, as allegedly indefinite in the recitation of certain terms and for antecedent basis. Applicants submit that the rejections under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph are rendered moot by way of the instant claim amendments and claim cancellations.

For example, claim 22 is amended herein to remove the recitation of the term “(non-yeast)”. With respect to rejected claims 29 and 30, claim 22 is amended herein to provide antecedent basis for “the first or second promoters”. Claim 31 is amended herein to recite “diploid *Pichia* cells”, which finds antecedent basis in claim 22. Claim 32 is amended herein to change the dependency of the claim to depend from claim 31, thereby addressing the antecedent basis for the phrase “said production media”. Similarly, claims 33 and 34 are amended herein to change the dependency of these claims to depend from claim 32, thereby addressing the antecedent basis for the phrase “said minimal media”. Claim 35 is amended herein to provide a numerical cell density value. Claims 45-47 are cancelled herein without prejudice or disclaimer, thereby rendering moot the rejection of these claims. Claims 54 and 55 are amended herein to provide a reference point from which the expression level is measured. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph.

**Conclusion**

An indication of allowance of all claims is earnestly solicited. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

HUNTON & WILLIAMS LLP

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By: 

Robin L. Teskin  
Registration No. 35,030

Robert C. Lampe, III  
Registration No. 51,914

Hunton & Williams LLP  
Intellectual Property Department  
1900 K Street, N.W., Suite 1200  
Washington, DC 20006-1109  
(202) 955-1500 (telephone)  
(202) 778-2201 (facsimile)